Development of Static Tracers for Myocardial Perfusion Imaging by MRI

Timothy F. Christian, MD
University of Vermont
Baird 191 MCHV
111 Colchester Ave
Burlington, VT 05495
802-847-2653

timothy.christian@uvm.edu

Development of Static Tracers for Myocardial Perfusion Imaging by MRI. Christian TF, Aletras AH, University of Vermont and the National Institutes of Health.

Summary: Current first pass MR stress Gd-based perfusion protocols are suboptimal due to the need to rapidly acquire images encompassing the LV in a short time frame. We propose to study contrast agents that are retained within the cardiac myocyte, thus allowing acquisition of images with higher resolution and SNR. There are certain kinetic principles which must be met for such a tracer but parallels exist in SPECT imaging.

Background: First-pass myocardial perfusion imaging by MRI remains a clinically unsatisfactory exam. There are four major shortcomings to the current approach: 1) The necessity of pharmacologic stress; exercise duration, the replication of symptoms with exercise and the electrocardiographic response are all lost with the reliance on vasodilator stress. These variables have been shown to have prognostic value equal to that of SPECT perfusion imaging when the resting ECG is normal and add to the overall perfusion interpretation. 2) Pharmacologic stress in the magnet is cumbersome, difficult to monitor safely, and magnet-time consuming. 3) First pass images, regardless of sequence, are of low signal and contaminated with artifact from the necessity of rapid gradient switching necessary to image multiple slices within 1-2 cardiac cycles and local field heterogeneity from the transit of the bolus. This makes interpretation challenging. 4) Different LV locations are imaged at different phases of the cardiac cycle

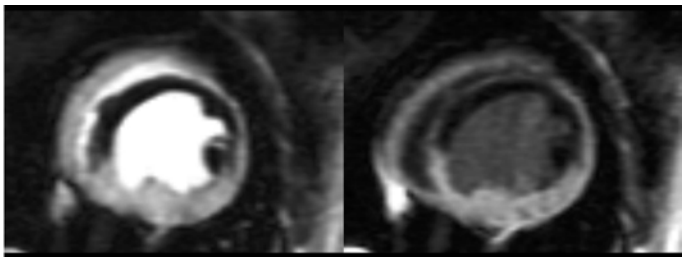
Purpose: To develop a "sticky" perfusion contrast agent much like the SPECT isonitrile compounds which are efficiently extracted and retained in the mitochondria of myocytes. Such a contrast agent would allow stress to be performed remote from the magnet (which allows the use of a treadmill or pharmacologic stress and closer monitoring). The images could be acquired at much higher spatial resolution and signal intensity, as the need for speed would be eliminated. Patient through-put would increase.

Design: Such an agent should contain the following properties:

1. Efficiently extracted by cardiac myocytes within 1-2 passes.
1. Extraction linearly related to myocardial blood flow to a minimum of 3ml/min/g.
2. Minimal myocardial washout over 30 minutes from injection.
3. Provide adequate myocardial enhancement and CNR for visual interpretation.
4. Not interfere with conventional Gd-DPTA delayed hyper enhanced imaging for viability.

There has been early experience with Manganese (see right) but it is too toxic for rapid injection during stress.

Conclusion: Widespread utilization of cardiac MR stress will not occur until such a contrast agent, which allows stress outside of the magnet, is developed.



$MnCl_2$ injected in a pig model of coronary occlusion. Left) SAX slice during initial injection with LAD occlusion and high blood pool level. Right) 30 minutes later. While the blood pool signal has dropped, myocardial enhancement remains high and the occlusion zone is still easily seen with a resolution allowing discrimination of subendocardial from tramsmural perfusion. Pulse sequence is gradient-echo inversion recovery imaged at every 4^{th} R-R interval